CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Proposed Policy for For-Profit Organizations

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I. Summary

For-profit awardees will own any intellectual property made as a consequence of CIRM funding. As is the case for non-profit grantees, for-profit awardees are expected to file annual reports, notify CIRM of press releases, publish results of CIRM-funded research and share biomedical materials described in publications. CIRM for-profit awardees may license CIRM-funded patented inventions to third parties. In that event, for-profit awardees are subject to licensing requirements similar to those required of non-profit grantees. If a for-profit awardee chooses to develop products for public use as a consequence of CIRM funded research, the State of California is entitled to a share of revenues after successful commercialization of the product. For-profit awardee organizations will provide a plan to provide access (at the time of commercialization) to resultant therapies for uninsured California patients, and will provide to patients whose therapies will be purchased in California by public funds the products at a discount price. CIRM retains march-in rights in the event that the awardee organization or its licensee of a CIRM-funded patented invention fails to comply with agreed upon terms aimed to bring CIRM-funded research projects to public use. CIRM may refer alleged violations of terms and conditions to the Office of the Attorney General of California for investigation and enforcement.

II. Introduction

Historically, the involvement of the for-profit research sector has been essential for the discovery and development of medical therapies and diagnostics. The California Stem Cell Research and Cures Act provides for the funding of for-profit research organizations (companies) in California to advance the development of products for public use. This proposed policy follows the CIRM Intellectual Property Policy for Non-Profit Organizations, approved by the Independent Citizens Oversight Committee on February 10, 2006, and is intended to provide terms and conditions to for-profit recipients of CIRM grants. There are no extant policy models that capture in entirety the intent of the State of California in its objectives to fund the for-profit research sector and provide a return to the state. As a consequence, this proposed policy is a unique synthesis of best practices and recommendations from funding agencies and foundations around the world.

Because for-profit research organizations are eligible to receive contracts, grants and loans, they are referred to as "awardees".

With successful examples of private, federal- and state-sponsored programs as guides, CIRM will support both non-profit and for-profit organizations as it executes its scientific strategic plan aimed to improve human health through the funding of stem cell research in California.

III. Background

Public-private partnerships involving research and development activities among industry, government, and universities can play an instrumental role in introducing key new technologies and valuable products to the commercial marketplace. Experience shows that partnerships involving government participation in research and development activities with industry, universities, and government laboratories can greatly facilitate the translation of basic research discoveries to products with societal benefits.

The mission of the CIRM is to foster and promote stem cell research with the aim of improving human health. A secondary goal is to strengthen California's biotechnology industry and create collateral economic benefits such as high-paying jobs and increased tax revenues. CIRM believes that the funding of commercial research organizations focused on stem cell-related projects is a key component to achieving the overall mission of the Institute. Increased interest by the commercial research sector in stem cell-related

research projects and the successful translation of basic research discoveries into commercial products for public use are primary success indicators (among others) that can be used by CIRM to track benefits of commercial sector funding.

To achieve the goal of commercialization of stem cell research-related products , CIRM will fund for-profit (commercial) research institutions in California via options that include contracts, grants and loans.

a. Public – Private Partnerships

A public-private partnership can be defined as an agreement in which one or more private sector companies are funded through a partnership with government. Federal, state and local government agencies or combinations of these types of agencies pursue public-private partnerships for many reasons in varied disciplines from national defense to biomedical research.

From its inception, the United States (US) has benefited from successful public-private partnerships for projects such as infrastructure construction to weapons production. In the post-Cold War period, cooperation between government and private industry was broadened to include knowledge generation and technology development through a variety of mechanisms. Current partnerships frequently involve direct support for research and development carried out by private firms, often in cooperation with universities or national laboratories. Partnerships have represented and continue to represent a pragmatic means of achieving government goals and exploiting technological opportunities that benefit the public.

Private investment to develop new technologies can be impeded by factors such as project scale and cost, dispersed expertise, and technical and commercial risk, even if these investments offer the prospect of substantial benefits to the company, the industry as a whole, and to society. By helping firms to overcome these barriers to investment, public-private partnerships can contribute to the development of industrial processes, products, and services that might not otherwise arise, and in this way help address government missions and generate greater public benefit.

Public private partnerships can address investment barriers presented by workforce challenges. Developing new technologies often require collective action, and partnerships can be a means of bringing together the components necessary for socially valuable innovation. New technologies often involve investments in combinations of technologies that may remain unexploited in companies. Joint research activities can facilitate the cooperation necessary to achieve the commercial potential of these technologies.

Partnerships can also encourage firms to undertake socially beneficial research and development (R&D). The return on R&D investment, even for promising technologies, can be perceived to be too low when risks related to technical development and commercialization are seen as substantial. Firms may not invest in R&D when they do not expect to be able to capture adequate revenue from the resulting innovations. Sharing the financial burden can decrease risk and help realize the potential of projects with high social impact but low return on investment.

Reduced R&D investments by private firms can also occur when they find it difficult to assign or enforce intellectual property rights, lowering expectations for returns on investments.

Each of these factors can influence decision-making processes with regard to investments in new products or processes that may be beneficial to the firm itself, the industry as a whole or society. Decisions regarding participation in public private partnerships are dependent on many variables, including the maturity of a company and the type of partnership under consideration.

b. Types of Public-Private Partnerships

Although many types of public-private partnerships exist, the National Research Council has focused on three of them in their 2002 report Government-Industry Partnerships for Development of New Technologies:

- ***Industry consortia:*** *In an R&D consortium a certain portion and type of a participating company's R&D is funneled into a separate organization where it is carried out collectively and where the research results are shared among the member firms. Consortia are particularly useful in the case of high-spillover technologies, where each firm may be reluctant to contribute to the production of goods that by their nature become widely available to others at little or no cost. In a consortium, firms can lower R&D costs or increase R&D efficiency while continuing to compete privately through their own product-related R&D programs. The role for government in the case of industry consortia is to legally enable this cooperation and when appropriate contribute funding and/or research facilities (e.g., national laboratories) to advance research on technologies of mutual interest.*
- ***Innovation funding:*** *Small businesses often face major constraints in bringing innovations to market. Financial markets often operate under conditions of imperfect information, often to the disadvantage of small firms working on less routine, more innovative projects. Small firms may also decide not to develop an*

innovation if they are not able to capture enough of the pay-off from this work—the so-called appropriability problem. Imperfections in capital markets can sometimes pose major challenges to small firms trying to bring their innovations to market. Federal partnerships provide awards that can help to address the early-stage funding requirements faced by firms engaged in the innovation-to-market process.

- ***Laboratory-based science and technology clusters:*** *Promoting innovation-led growth by encouraging knowledge clusters around the nucleus of national laboratories and research facilities is an important aspect of public-private partnerships in the United States. Traditional S&T (Science and Technology) parks are expected to diffuse knowledge and technology and thus provide an engine of growth for a region. In practice, however, the goals of these Science and Technology parks are often extensive, with imperfect definitions, and achievement can be correspondingly difficult to assess.*

Successful public-private partnerships are a result of the productive interactions of its players and the environment of the partnership, which in turn depends on government policies related to taxation, fiscal and monetary matters, education and training, trade promotion and expansion, regulatory policies (e.g., for anti-trust and the environment), intellectual property protection, government procurement, and export control. These policies can all directly affect the processes of innovation and commercialization.

As with other successful ventures, the quality of industry leadership in a public-private partnership is of critical importance. Industry typically supplies valuable domain-specific technological expertise and management experience to the public-private partnership. For government programs that fund innovation, identifying effective management teams is an important part of the grant and evaluation procedures. A continued commitment to monitoring the progress of the management team as it oversees the funded research project remains a significant responsibility for many government partnership divisions after awards are made.

c. Federal Government Approaches to Public-Private Partnerships

Substantial investment in research and development—both public and private—is a prerequisite for sustaining US economic growth in a global economy (National Research Council, *Allocating Federal Funds for Science and Technology*, Washington, D.C.: National Academy Press, 1995.) Governments have developed a variety of mechanisms designed to support R&D industries including policies for trade regulations designed to protect domestic products from foreign competition and tax rebates intended to stimulate the export of selected domestic products. Major financial support is sometimes overtly provided through direct grants, loans, and equity investments; more indirect support can also be provided through mechanisms such as tax deferral.

In addition to its prominent role in supporting research in academic sectors, the US federal government maintains a significant commitment to effective public-private partnerships. In the 1980s the US responded to a perceived loss in national competitiveness by encouraging greater cooperation among industry and between industry and government. Congress enacted legislation during this time period to provide new mechanisms for government – industry collaboration; a summary from the National Academies report on the Advanced Technology Program follows:

- ***Stevenson-Wydler Technology Innovation Act (1980)*** *Required federal laboratories to facilitate the transfer of federally owned and originated technology to state and local governments and the private sector. The Act includes a requirement that each federal lab spend a specified percentage of its research and development budget on transfer activities and that an Office of Research and Technology Applications (ORTA) be established to facilitate such transfer.*
- ***Bayh-Dole University and Small Business Patent Act (1980)*** *Permitted government awardees and contractors to retain title to federally funded inventions and encouraged universities to license inventions to industry. The Act is designed to foster interaction between academia and the business community. This law provides, in part, for title to inventions made by contractors receiving federal R&D funds to be vested in the contractor if they are small businesses, universities, or not-for-profit institutions.*
- ***Small Business Innovation Development Act (1982)*** *Established the Small Business Innovation Research (SBIR) Program within the major federal R&D agencies to increase government funding of research with commercialization potential in the small high-technology company sector. Each federal agency with an R&D budget of $100 million or more is required to set aside a certain percentage of that amount to finance the SBIR effort.*

- ***National Cooperative Research Act (1984)*** *The National Cooperative Research Act of 1984 eased antitrust penalties on cooperative research by instituting single, as opposed to treble, damages for antitrust violations in joint research. The Act also mandated a "rule of reason" standard for assessing potential antitrust violations for cooperative research. This contrasted with the per se standard by which any R&D collusion was an automatic violation, regardless of a determination of economic damage.*
- ***Federal Technology Transfer Act (1986)*** *Amended the Stevenson-Wydler Technology Innovation Act to authorize Cooperative Research and Development Agreements (CRADAs) between federal laboratories and other entities, including state agencies.*
- ***Omnibus Trade and Competitiveness Act (1988)*** *In addition to establishing a Competitiveness Policy Council designed to enhance U.S. industrial competitiveness, the Act created several new programs (e.g., the Advanced Technology Program and the Manufacturing Technology Centers) housed in the Department of Commerce's National Institute of Standards and Technology and intended to help accelerate development, commercialization, and application of promising new technologies and improve manufacturing techniques of small and medium-sized manufacturers.*
- ***National Competitiveness Technology Transfer Act (1989)*** *Part of the Department of Defense authorization bill, this act amended the Stevenson-Wydler Act to allow government-owned, contractor-operated laboratories to enter into cooperative R&D agreements.*

d. Federal Research Agreements

The scope of federal cooperative activity is vast and includes programs such as the national manufacturing initiative, the National Science Foundation's (NSF) Engineering Research Centers, NSF's Science and Technology Centers, NIST's Manufacturing Extension Partnership Program and Advanced Technology Program, and the multi-agency Small Business Innovation Research Program, which will be discussed in more detail later in this document.

The federal government currently makes use of a variety of mechanisms to promote research and development in the commercial sector in the US. Cooperative Agreements, CRADAs and Sponsored Research Agreements are some of the many types of funding arrangements sanctioned by the federal government to support the commercial research sector and industry-university partnerships.

Cooperative agreements are used to fund both the non-profit and for-profit research sectors. In brief, a cooperative agreement differs from a grant in the level of federal programmatic involvement with the recipient during the performance period; a cooperative agreement is used when substantial involvement by the federal government is anticipated, frequently for complex projects or projects where networks of sites around the country undertake a standard clinical protocol and contribute data to a central data coordinating center. Cooperative agreements are routinely used by the NIH to support commercial researchers in clinical development research.

University-industry cooperation has also increased, with a significant percentage of university R&D costs now provided by industry. Sponsored research agreements are agreements between non-profit researchers and commercial entities in which non-profit researchers receive funding or other consideration to support their research in return for preferential access and/or rights to intellectual property deriving from their research results. The commitment of the federal government to the Bayh-Dole Act provides for collaborations between government sponsored researchers and industry partners.

National laboratories now have extensive cooperative agreements with industrial firms in the form of CRADAs. CRADAs are agreements between one or more federal laboratories and one or more non-federal parties under which the federal government, through its laboratories, provides personnel, services, facilities, equipment, intellectual property, or other resources with or without reimbursement (but not funds to non-federal parties) and the non-federal parties provide funds, personnel, services, facilities, equipment, intellectual property, or other resources toward the conduct of specified research or development. The Stevenson-Wydler Act of 1980 and the Technology Transfer Act of 1986 were amended in 1989 to allow industry-operated federal labs to participate, these laws stimulated hundreds of CRADAs. Between 1989 and 1995, the Department of Energy alone signed more than 1,000 CRADAs. Some of the requirements of these agreements posed daunting challenges for small businesses, most notably a component termed the “fair pricing clause”. This clause stated "that there be a reasonable relationship between the pricing of a licensed product, the public investment in that product, and the health and safety needs of the public. Accordingly, exclusive commercialization licenses granted for NIH/ADAMHA[*] intellectual property may require that this relationship be supported by reasonable evidence." The ambiguity of the term “fair pricing” and the fear that this clause could be used to require companies to justify their pricing strategies of resultant products resulted in a chilling effect on collaborations between industry and the NIH. After evidence suggested that the “fair

[*] Alcohol, Drug Abuse and Mental Health Administration

pricing" policy created a disincentive toward the goal of developing therapies, the NIH abandoned the "fair pricing" clause in 1995 to enable technology transfer as the necessary step to achieve government goals. A rebound in the number of NIH CRADAs executed after 1995 suggests that the abolition of the "fair pricing" clause has had a positive effect on technology transfer of federally funded research discoveries to the for-profit research sector. CRADAs continue to evolve and contribute to significant technological developments on the path to the commercialization of early discoveries.

(See appendix 1 for a summary of funding source information.)

i. Small Business Innovation Research Program

The 2004 National Academies Press report *SBIR Program Diversity and Assessment Challenges: Report of a Symposium* provides a brief history of the federal government's Small Business Innovation Research (SBIR) program:

> *The concept of early-stage financial support for high-risk technologies with commercial promise was first advanced by Roland Tibbetts at the National Science Foundation (NSF). As early as 1976, Mr. Tibbetts advocated that the NSF should increase the share of its funds going to small business. A White House Conference on Small Business was held in January 1980 under the Carter Administration. The conference's recommendation to proceed with a program for small business innovation research was grounded in:*
> - *Evidence that a declining share of federal R&D was going to small businesses;*
> - *Broader difficulties among small businesses in raising capital in a period of historically high interest rates; and*
> - *Research suggesting that small businesses were fertile sources of job creation.*

Under the Reagan administration, Congress passed the Small Business Innovation Research Development Act of 1982, which established the SBIR program. Congress intended the Small Business Innovation Research Development Act of 1982 to meet four goals:

- Stimulate technological innovation
- Use small businesses, established reservoirs for innovative technologies, to meet US R&D needs
- Encourage participation of minorities and disadvantaged persons in technological innovation
- Attract private capital to commercialize the results of federal research

The Small Business Innovation Research Development Act required that federal agencies with R&D budgets in excess of $100 million set aside 0.2 percent of their funds for SBIR. This amount totaled $45 million in 1983, the program's first year of operation. Over subsequent years, the set-aside continues to grow and is now 2.5 percent.

Federal agencies with R&D budgets over $100 million are the Department of Defense, Department of Energy, Department of Health and Human Services, National Aeronautics and Space Administration, National Science Foundation, Department of Homeland Security, US Department of Agriculture, Department of Commerce, US Department of Education, US Environmental Protection Agency, and the US Department of Transportation.

Since 1983, the federal agencies have collectively invested more than $12 billion in SBIR projects. The NIH investment exceeds $2.5 billion.

ii. Small Business Technology Transfer Program

The smaller Small Business Technology Transfer (STTR) program is focused on industry and the academic and non-profit research community, and strives to forge alliances such as university-private sector partnerships. STTR reserves a specific percentage of federal R&D funding for award to small business and nonprofit research institution partners. Small businesses must be a for-profit American-owned and independently operated firm with 500 or fewer employees. The nonprofit research institution must also meet certain eligibility criteria; it must be located in the US and qualify as a nonprofit college or university, domestic non-profit research organization, or federally funded R&D center.

Five of the eleven agencies that participate in SBIR program also participate in STTR Program. The Department of Defense, Department of Energy, Department of Health and Human Services, National Aeronautics and Space Administration and the National Science Foundation participate in the STTR program, and are required to set aside 0.3 percent of their R&D budgets for small business/non-profit research partnerships.

<u>SBIR and STTR programs are similar and structured in three phases:</u>

The three phases of SBIR and STTR grants are termed Phase I, II and III (not to be confused with the similarly named FDA Phase I, II and III clinical trials).

> Phase I – a feasibility study in which award winners undertake a limited amount of research aimed at establishing an idea's scientific and commercial promise, approximately $100,000.

Phase II - funds more extensive R&D to further develop the scientific and technical merit and the feasibility of the research idea, normally up to $750,000. Only Phase I award recipients are eligible for Phase II awards.

Phase III - does not involve SBIR/STTR funds, but is the stage at which grant recipients should be obtaining additional funds either from a procurement program at the agency that made the award, from private investors, or from the capital markets. The objective of this phase is to move the technology to the prototype stage and into the marketplace.

From a company perspective SBIR/STTR grants are attractive since there is no dilution of ownership or repayment required. Grant recipients retain rights to intellectual property developed using the awards, with no royalties owed to the government, though the government retains royalty free use for a period. However, administration of such grants within commercial research environments can present a distraction from other corporate operations relative to the investment.

From a government perspective, SBIR/STTR grants can help achieve agency missions as well as encourage knowledge-based economic growth. SBIR/STTR serves as a catalyst for the development of new ideas and new technologies to meet federal missions in health, transport, the environment, and defense, and provides a bridge between universities and the marketplace, encouraging local and regional growth. Also, by addressing gaps in early-stage funding for promising technologies, the program can help the US capitalize on its substantial investments in research and development. Since implementation of SBIR/STTR operations is carried out in agencies with quite distinct missions and interests (e.g. DARPA, NIH, NASA), there is significant variation in objectives and mechanisms (contracts versus grants).

There is no federal government repayment obligation for SBIR or STTR programs.

iii. Advanced Technology Program

Established in 1988 under the Reagan Administration and first funded under the George H.W. Bush Administration, the Advanced Technology Program (ATP) represented one component of the US government's efforts to restore and enhance the competitiveness of the US economy. Administered by the Department of Commerce's National Institutes of Standards and Technology, ATP was established to provide cost-shared funding to industry to accelerate the development and broad dissemination of challenging, high-risk technologies that promise broad-based economic benefits for the nation. The 2001

National Academy Press report *The Advanced Technology Program: Assessing Outcomes* describes ATP as aimed to support:

- *emerging and enabling technologies facing technical challenges, which, if overcome, would contribute to the future development of new and substantially improved products, industrial processes, and services in diverse areas of application;*
- *technologies whose development often involves complex "systems" problems requiring a collaborative effort by multiple organizations;*
- *technologies that, because of their risk, or because firms are unable to fully capture their benefits, are unlikely to be developed by individual firms, or may proceed too slowly to compete in rapidly changing world markets without the impetus of an ATP award.*

The ATP provides a leading role for industry, balanced by government and outside expert review in the creation of new technologies with broad "spillover" potential that may benefit society. Companies conceive, propose, co-fund, and execute all of the projects; ATP identifies the most promising projects and contributes to their development on a cost-shared basis.

Research priorities for ATP are high-risk, early stage and set by industry. ATP awardees own any resultant intellectual property that may arise from ATP funding. ATP does not provide follow-on funding and does not fund product development stages.

Three components contribute to ATP's success as an accelerator of the development of innovative technologies for broad national benefit through partnerships with the private sector: rigorous peer review, encouragement of dissemination of results and performance assessment.

From 1990 to 2004, the range of ATP awards was $434,000 to $31 million, with a total of $2.3 billion committed. There are no direct repayment expectations associated with ATP funding.

e. State Government Approaches to Public-Private Partnerships

The federal government is not unique in its commitment to the use of public-private partnerships as a means to achieve government objectives; state governments also routinely collaborate with private businesses to enable projects in various sectors from infrastructure construction to biomedical research.

There are many examples of state-sponsored efforts to promote technology transfer to the commercial sector, and different states have adopted different approaches. This policy

does not strive to be inclusive but rather focuses on a few detailed examples to illustrate exemplary approaches.

i. Maryland

The Maryland Technology Development Corporation (TEDCO) was created by the Maryland General Assembly in 1998 to "(1) Assist in transferring to the private sector and commercializing the results and products of scientific research and development conducted by colleges and universities; (2) Assist in the commercialization of technology developed in the private sector; and (3) foster the commercialization of research and development…to create and sustain businesses throughout all regions of the State" and "to promote entrepreneurship and the creation of jobs in technology-related industry by establishing and operating effective incubators throughout the State that provide adequate physical space designed, and programs intended, to increase or accelerate business success in the field of technology." In 2001 TEDCO was further authorized to promote entrepreneurship and job creation by establishing and operating business incubator facilities and programs. Some of TEDCO's programs are directly focused on improving technology transfer and growing technology-based companies:

> The University Patent Support Program aims to help universities secure patents for their inventions.
>
> The University Technology Development Fund provides up to $50,000 to universities to make their technologies more attractive to licensees.
>
> The Maryland Technology Transfer Fund provides initial non-equity investments of up to $75,000 per company to help defray the costs of initial transfer or technology from or co-development of technologies with universities and federal laboratories in Maryland. These awards have payback obligations in the event of company revenue; one company has converted its payback obligation to equity in a venture capital investment round.
>
> The Federal Laboratory Partnership Program provides a subsidy of up to $20,000 to companies that collaborate in a formal agreement with a federal lab with which TEDCO has an established partnership.
>
> The Incubator Development Fund is designed to develop and grow technology-based companies around the state. TEDCO provides matching funds (1:1) to qualified groups interested in developing incubator programs for capital development. Payback is expected, and is used to fund other incubator activities.

The Working Capital Loan Fund provides loans to early stage technology-oriented companies located in the state of Maryland. Loans of between $15,000 and $50,000 are available to be used for working capital in order to assist a company with expansion, market entry, or other initiatives. Rates are at or below market rate and the loan term is normally 3 to 5 years with a minimum term of 6 months. Companies are required to participate in a Maryland incubation program.

ii. Pennsylvania

The Ben Franklin Partnership was created by the Pennsylvania General Assembly in 1982, re-authorized as the Ben Franklin/IRC Partnership in 1993, and reauthorized as the Ben Franklin Technology Development Authority in 2001. The overall mission of the Authority is to assist Pennsylvania in developing a robust, globally competitive economy through:

- High value added products, processes, and services;
- Innovative integration of technology and Pennsylvania human resources;
- World-class Pennsylvania-based technology and business, financial, and information services; and investing in economic, community, and university based innovation

The four Ben Franklin Technology Partners created throughout Pennsylvania were designed to develop partnerships to:

1. Help companies with high growth potential to form and grow through the development and commercialization of innovative products and services, and to reach a stage in their development that will facilitate the attraction of follow-on funding;

2. Help established companies to develop and innovatively apply new technologies and practices that make them more competitive in the global market economy; and

3. Facilitate and support the availability of services, technical assistance, and collaborative activities throughout Pennsylvania to enhance the community's capacity to support modern business.

Policies for ownership of patents are driven by contributions made by both the participating academic institution and the private industry participant if joint inventions are made. For projects that do not involve an academic institution, the participating private sector company(ies) retain patent ownership.

Ben Franklin Technology Partners are encouraged by the Development Authority to enter

into royalty, equity or other repayment payback agreements with participating companies and academic institutions on the condition that agreements do not burden a company to a point that hinders their growth, development or continued viability. Where a royalty agreement with a private company involves a payback to the participating university, a portion of the royalty payment will also be made to the Partner.

Over 20 years, Ben Franklin Technology Partners have funded thousands of companies in Pennsylvania with funding in the range of $5,000 to $250,000 (although sometimes much higher). Grants and loans are used with payback terms included; occasionally loans are converted to equity positions.

iii. California

University of California (UC) Discovery Grants (founded in 1996) provide up to $60 million per year in state, university and industry funds for new research partnerships. The goals of UC Discovery grants are:

- To promote and support high quality, early stage research with grants funded by UC and the State, with matching support by California businesses
- To speed the utilization of research discoveries for public benefit, by facilitating technology transfer
- To support the training environment that prepares California's future workforce and industry leaders
- To advance understanding of the role of science and technology in California's increasingly knowledge-based economy
- To assess and communicate the social and economic impact of research and education

Benefits to the State of California are defined as:

- Accelerated delivery of public benefits from UC research and education
- Promotion of highly meritorious research that addresses California's needs
- Increased investments in research and education at a time of unstable federal funding
- Increased competitiveness of California businesses

Benefits to sponsors are listed as:

- Immediate leveraging of R&D funds
- California and Federal Tax Credits
- Access to UC’s world class faculty and research resources
- Access to UC’s outstanding students

- Expansion of company R&D capacity through partnership with UC researchers
- Participation in research requiring multidisciplinary teams
- Intellectual Property rights

UC researchers benefit from:

- Up to 4 years of funding and support for research projects
- Training opportunities and funding for students and post-doctoral researchers
- Special consideration for interdisciplinary and multi-investigator projects
- Frequent grant solicitations (three application rounds per year)
- Award notification within six weeks after deadline
- Online proposal submission minimizes paperwork

Roughly 185 California companies have participated in the UC Discovery Grant biotechnology program to date. Hundreds more have received grants in the fields of communications and electronics.

Previous grants have ranged from $50,000 to $3 million. No payback terms are required.

The California Special Research Programs (SRP) are three state-funded research programs that target high-priority health issues in California: HIV/AIDS, breast cancer, and tobacco-related disease. The goals of scientific research supported by these programs are to enhance understanding of the causes of these diseases, and to develop more effective approaches to preventing and treating them. Although the University of California administers the three programs as a public service, grant awards are not restricted to UC scientists. SRP has awarded grants in the areas of public health, public policy, the law, epidemiology, clinical and behavioral medicine, and basic biomedical science (e.g., cellular and molecular biology, immunology, pathology, virology). In 1994 enabling legislation (AB 478) allowed the California Breast Cancer Research Program to provide funding to for-profit research organizations. No payback terms are required.

f. Other State Stem Cell Programs

To date, California, Connecticut, Illinois, Maryland and New Jersey have established programs for financial support of embryonic stem cell research. Of them, California, New Jersey and Maryland are the states that fund or plan to fund the for-profit research sector. Connecticut and Illinois have limited eligibility for funding to non-profit research organizations.

The New Jersey Commission on Science and Technology reported $21 million in appropriations to the Stem Cell Institute of New Jersey (a research facility) and for stem cell research grants in fiscal year 2005 and 2006. The Stem Cell Research Grant Program

awarded its first research grants in December 2005, totaling $5 million, to 17 research teams at university, non-profit institutions and corporate laboratories from among the 71 applications received. Awards were approximately $300,000 each. Awards carry a 1 percent royalty payback expectation on net sales of any product or services arising directly out of a research project or developed based on intellectual property created. Also expected is a royalty 1 percent of any amounts received (other than net sales) by a qualified research institution from a third party in connection with products, services or intellectual property arising directly out of a research project.

The Maryland budget for fiscal year 2007 includes $15 million for the newly created Maryland Stem Cell Research Fund. Intellectual property rights will be decided by a committee to be established. Fund management and administration will be provided by TEDCO.

Connecticut's Stem Cell Research Program has appropriated not less than $10 million each year for ten years starting in 2006. For-profit research organizations are not eligible to apply for grants in the Connecticut program. Connecticut reported its first allocation of $19.78 million in awards to three universities on November 21, 2006. The Connecticut Stem Cell Research Advisory Committee requires applicants to propose arrangements concerning financial benefits to the State of Connecticut as a result of any patent, royalty payment or similar rights that may result from any research made possible by the grant. As stated in the Connecticut Stem Cell Research Grants Program proposal instructions, a minimum return to Connecticut of 5 percent share of resultant royalties and other income is required.

Illinois established the Illinois Regenerative Medicine Institute (IRMI) with the transfer of $10 million by the governor within the Illinois Department of Public Health. Illinois awarded $10 million in grants to 10 "hospitals and universities" in April 2006, and $5 million in grants to 7 institutions in August 2006. Grants ranged from $250,000 to $2 million. Terms for intellectual property rights are defined in grant awards.

g. Relevant Research

In addition to the federal and state government agencies mentioned above, many additional granting entities and experts in the fields of technology transfer, economic development and government policy were contacted in the course of the research for this policy. Among the foundations and granting entities surveyed were the Howard Hughes Medical Institute, Gates Foundation, Wellcome Trust, Cancer Research UK, International AIDS Vaccine Initiative, Juvenile Diabetes Research Foundation, Cystic Fibrosis Foundation, American Cancer Society, American Heart Association, Myelin Repair Foundation and the Multiple Myeloma Research Foundation. Additional relevant

research was conducted through interviews and literature/web searches at the California Council on Science and Technology, the National Academies, the US Department of Commerce, the Food and Drug Administration (FDA) and the Semiconductor Research Corporation. Several individuals of the for-profit research sector from "stem cell" and "non-stem cell" companies were interviewed, as were representatives from venture firms.

h. The Commercial Sector and its Role in the Commercialization of Biomedical Research Discoveries

While academic settings appear to be ideal for basic research, non-profit institutions have not traditionally been effective in their efforts to translate the fruits of basic research to products that improve human health. In contrast, the for-profit sector has proven over the last half century to be remarkably successful in making the results of scientific investigations available for public use. A recent report shows that the majority of FDA approvals for new medicines have their origins in biotechnology R&D rather than university inventions. See Table 1 for a breakdown of FDA approvals originating from biotechnology R&D and university inventions in the 1998-2003 time period.

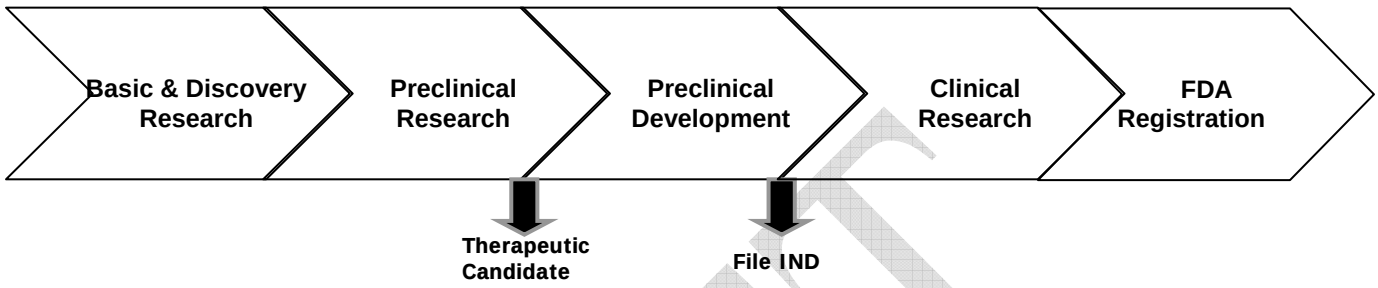
Table 1: from The Origins of New Drugs, **Nature Biotechnology** 2005, 23 (5) 529-530

Category	1998	1999	2000	2001	2002	2003	1998 - 2003
FDA Approvals							
Total	34	34	28	26	22	26	170
No. originating from biotech R&D	14	11	9	8	7	13	62
No. based on university invention	4	8	4	3	2	5	26
University inventions licensed directly to pharma company	1	2	2	0	0	0	5
New Molecular Entities (NMEs)							
Total	29	33	26	21	15	20	145
No. originating from biotech R&D	10	10	7	4	2	7	40
No. based on university invention	4	7	4	1	1	4	21
University inventions licensed directly to pharma company	1	2	2	0	0	0	5
New Biological Entities (NBEs)							
Total	5	2	2	5	7	6	26
No. originating from biotech R&D	4	1	2	4	5	6	22
No. based on university invention	0	1	0	2	1	2	6

In the area of biomedical research, for-profit organizations provide expertise and facilities necessary for the discovery and development of therapeutic and diagnostic products typically not present in non-profit research institutions. Examples of such capabilities include high-throughput screening, laboratory animal facilities specializing in efficacy and *in vivo* pharmacology testing, process development, scale up and manufacturing, regulatory expertise, marketing and sales. The discovery and development of a new therapeutic entity is a consequence of the progression of a project through defined stages of long and expensive path, one that is possible due to highly skilled interdisciplinary

teams and significant private sector investment. See Figure 1 for a diagram of schematic stages that may be associated with the development of a cellular therapy.

Figure 1: Stages of Cell Therapy Development



- Reprogramming
- Stem cell identity
- Self renewal
- Niche/Environment
- Mechanisms of stem cell function
- Differentaition
- Cancer stem cells
- Immune rejection/Tolerance

- Documentable Cell Line Derivation
- Cell line characterization
- Culture conditions for growth, expansion and differentiation
- Development of cryopreservation methods
- Lineage analysis
- Assay development

- Produce cells for in vivo/in vitro testing
- In vitro testing and characterization
- Develop of scalable serum and feeder free methods to grow and cells
- Delivery methods
- Methods for in vivo tracking and monitoring
- In vivo testing (show preclinical proof of concept)
- Pilot safety
- Immune tolerance/rejection
- Clinical strategy

- Prepare Master and Working cell banks
- Develop scalable processes for cell production, purification
- Produce GLP cell product and GMP cell product
- Assays to assess purity, potency and identity
- Long term cell stability
- IND supporting pharmacology and PK/PD (activity, dose, homing, maintenance of function)
- IND-Supporting Safety (tumorigenicity, toxicity)
- Clinical protocol

- Pilot Safety
- Dose, delivery, regimen studies
- Evidence of therapeutic effect (proof of principle)

- Phase III clinical trials
- Build manufacturing capabilities
- Manufacturing/scale-up/packaging

Roughly drawn, the stages of therapy development can be defined as discovery, preclinical studies and development, and costs of the stages increase significantly from discovery to development. The discovery stage is the start of the process, where an idea for a therapy is usually followed by early feasibility studies and a convincing link between the idea and its therapeutic potential. Discovery is where projects with therapeutic potential are discovered or designed. For example, if a scientist proposes that an antibody targeted to a cancer cell will be effective in the treatment of a form of cancer, the discovery stage will be focused on whether a cancer cell is different from a normal cell in a way that can be interrogated experimentally, whether that difference is due to a protein that can be targeted by an antibody that has a desired activity, and whether that active antibody can demonstrate efficacy in a relevant animal model of cancer. The discovery stage can be of varying lengths of time depending on how well understood the biological basis of disease is, and how successful the screening efforts are to identify a promising therapeutic agent for further preclinical investigation.

Preclinical studies are largely done in animals under Good Laboratory Practice (GLP) conditions with some supporting cellular analyses, and are designed to understand how the therapeutic agent behaves in a mammal. It is during this stage of research where important safety and pharmacologic data is generated, and where some liabilities of the therapeutic agent can be discovered in metabolism and toxicity studies. Is the agent absorbed through the gut? Is the agent distributed to all tissues or does it not cross the blood brain barrier? Is the agent metabolized into secondary molecules that might have better activity or a toxic liability? Is the agent excreted through the kidneys or via another route? Pharmacological parameters such as half life of the agent in the bloodstream can help understand proper dosage estimates for improved efficacy. Maximum tolerated doses are determined such that the therapeutic index (the difference between the minimum effective dose and the maximum tolerated dose) can be calculated to inform clinical trials. Given costs involved, failures in preclinical studies are preferable to failures during clinical trials, so considerable effort is spent in designing predictive preclinical studies in animals so that clinical trials may be executed with only the most promising therapeutic candidates.

Development is typically the most costly stage of the therapeutic process and is comprised primarily of the completion of regulatory requirements of therapy licensing agencies, such as the FDA or the European Medicines Agency. Stringent testing in humans for safety and efficacy is required for approval, and these tests are termed clinical trials. A clinical trial protocol describes the objective, design, methodology, statistical considerations and organization of a clinical trial, including length of the study and what types of people may participate in the trial. Trials are commonly classified into four phases, with an agent progressing through all four stages over many years. If successful through the first three phases, a therapy will usually be approved for use.

Phase I trials are designed to assess the safety, tolerability, pharmacokinetics (what the body does to the therapeutic agent) and pharmacodynamics (what the agent does to the body) with a relatively small number of usually healthy participants (less than 100) and with doses that are chosen to be a small fraction of the dose that causes harm in animal testing. Dose-ranging experiments are normally done in Phase I such that doses for clinical efficacy can be refined.

Phase II studies are performed on larger groups (hundreds of people) and are designed to assess clinical efficacy of the therapeutic agent. Phase IIA studies are used to assess dosing requirements and Phase IIB studies are designed to study efficacy. Depending on the therapeutic indication under investigation, Phase I and Phase II studies maybe combined into a single trial that assesses both safety and efficacy. New therapeutic agents commonly fail in Phase II due to lack of efficacy or unacceptable side effects (toxicity).

Phase III trials are large (sometimes thousands of patients) and designed to determine the definitive efficacy of the therapy. These are the most expensive, time-consuming and difficult trials to design and run, especially for chronic illnesses. Statistical evaluation of the clinical trial data is required to ascertain whether efficacious results are significant, and if the frequency of side effects is acceptable given efficacious activity. Successful Phase III completion is followed by a the submission of a comprehensive report containing animal and human data, manufacturing procedures, formulation details and stability studies for consideration by the regulatory agency for marketing approval.

Phase IV trials involve post-launch safety surveillance to assess any long-term adverse effects over a larger patient population and timescale than was performed in Phase III. Such studies may be mandated by a regulatory agency or supported by a sponsoring company for competitive reasons.

In all, discovery, preclinical studies and clinical trials span many years and cost hundreds of millions of dollars. While the non-profit research sector can provide a significant head start in the discovery phase by identifying possible targets or pathways related to disease and plays a significant role in clinical development, the for-profit research sector is designed to translate early discoveries into successful therapies for use by the public by leveraging private funds and highly skilled interdisciplinary teams not found in academic environments.

i. Revenue Sharing Strategies in Brief

The for-profit research sector primarily uses funding to support discovery, preclinical and clinical development to advance toward commercialization of products for public use. There are a variety of sources of private funds available to companies, and virtually all of these expect a financial return on investment.

There are a number of ways that a company can provide a return on an investment, and frequently the strategy used is a function of the stage of the company at the time when the investment is made. Small private companies have different risk profiles than more mature public companies. Projects also vary in their risk profiles at various periods throughout their development; later stage projects tend to carry lower risk. Investments at different stages of a company's or a project's lifetime can "cost" a company more in the way of a return depending on how the investment is valued at the time it is made. Equity investments may be preferable under certain conditions over those requiring an immediate direct financial return. For example, private startup companies typically fund themselves by selling equity in the form of stock to venture capital firms. This offers the venture firm a longer prospect of financial return since stock in a private company cannot be converted to cash immediately. Other forms of remuneration may include royalties and milestone payments. Royalties are fixed annual fees or a percentage of product revenues, and are usually based on product success in the marketplace. Milestone payments are another form of direct remuneration and are made when the technology or product reaches a key stage in its path to successful development or commercialization.

Although typical financial return strategies may offer equity or stock components, such options are not appropriate for consideration for returns as a consequence of stem cell research funding for the State of California per the Constitution of California:

> *The credit of the State shall not, in any manner, be given or loaned to or in aid of any individual, association, or corporation; nor shall the State directly [or] indirectly become a stockholder in any association or corporation.*

Consequently, some of the successful revenue sharing strategies used by established granting agencies to share in successes from funding biomedical research (notably stock ownership) are not possible models for CIRM's consideration of revenue sharing options.

i. The federal government does not seek financial returns from awardees

The federal government does not seek remuneration in the event of successful commercialization of government-funded research projects from either non-profit or for-profit research sector awardees. It views the creation of knowledge, development of products for public use, increased tax revenues and economic growth as valuable outputs and do not seek direct financial return.

ii. Some states require commercial awardees to share revenues

Unlike the federal government, some state entities require recipients of public funds to repay the state in whole or in part, as described in some earlier examples. The California Special Research Program and the UC Discovery Grants program provide funding to for-profit research organizations without an expectation of repayment.

J. CIRM Mission

The primary purpose of CIRM is to support stem cell research with the goal of promoting the development of therapies and diagnostics for the improvement of human health.

CIRM Mission Statement:

> *To support and advance stem cell research and regenerative medicine under the highest ethical and medical standards for the discovery and development of cures, therapies, diagnostics and research technologies to relieve human suffering from chronic disease and injury.*

CIRM is committed to funding stem cell research with the understanding that based on historical data, only a small fraction of research funded by CIRM may give rise to projects that will be commercialized. However, CIRM is obliged to ensure that the fruits of CIRM-funded research are used and disseminated so that the understanding, diagnosis and treatment of human disease is maximized for the benefit of patients and the general population in California. Depending on the research project involved, this may be best achieved through the protection of intellectual property and commercial exploitation of patents.

CIRM funding will be aimed to enable companies to develop research projects into new healthcare applications, or license them to third parties to further develop the projects. As for non-profit awardees, CIRM assumes that for-profit organizations that are funded

by CIRM are in possession of appropriate permissions, licenses and certifications required to execute the research programs for which they have requested funding.

K. Policy Components

i. For-profit awardees will own CIRM-funded intellectual property

In recognition that the use and dissemination of CIRM-funded research should be maximized for the benefit of the public, CIRM will grant ownership of research findings, intellectual property and materials arising from CIRM-funded research to the commercial research organization awardees to facilitate the development of resultant products for public use.

ii. Reporting, press releases, publications, publication-related biomedical materials sharing

As is the case for CIRM non-profit grantees, for-profit grantees are expected to file annual reports to CIRM, notify CIRM of relevant press releases and include CIRM in media distributions of formal materials, publish their research findings and share publication-related biomedical materials such that research findings can be replicated by others. Future scientific research relies on the ability to replicate and extend past scientific research, and access to materials described in scientific articles enables this. It is customary for researchers to share materials described in scientific articles; some prestigious journals require sharing as a condition of publication of the article. The intent of the CIRM publication-related biomedical materials sharing requirement is to promote rapid progress in the field of stem cell research. If requests become onerous or are in direct conflict with the business of the awardee, for-profit awardees may appeal to CIRM for alternative arrangements.

iii. CIRM grants to for-profit organizations have an expectation of payback

Commercialization of stem cell research discoveries for public benefit is an expected outcome from CIRM funding. Current data suggest that discovery and development of a therapy can cost in excess of $800 million. Although CIRM is not expected to completely fund the discovery and development of a stem cell-related therapy from start to finish, state funding may contribute in substantial ways to the commercialization of a product.

The California Stem Cell Research and Cures Act anticipates a return to the State of California:

> *The ICOC shall establish standards that require that all grants and loan awards be subject to intellectual property agreements that balance the opportunity of the State of California to benefit from the patents, royalties, and licenses that result from basic research, therapy development, and clinical trials with the need to assure that essential medical research is not unreasonably hindered by the intellectual property agreements.*

Therefore, CIRM is expected to require that in the event of the creation of a revenue stream from commercialization of a CIRM-funded program, for-profit awardees will share a portion of such revenues with the State of California for deposit into the General Fund.

Returns to the State of California may take many forms, only some of which are relevant to the development of a sharing policy for for-profit awardee organizations. Direct financial payments to the State of California and the provision of resultant products to Californian patients under specific terms are the forms under consideration in this policy.

Given that most grants represent only a small fraction of the total funds needed to commercialize a product, a common theme of many biomedical research funding organizations that maintain payback expectations is consideration of the proportion of funding used to create the resultant product. Typically, this requires reporting of detailed calculations by the awardee to the funding entity to support claims made about proportional funds used in the commercialization of a product.

Awards to for-profit research organizations will be accompanied by specific agreements that describe payment expectations and time periods under which payments must be made. Such agreements will be individually negotiated with the aim of ensuring that companies are not subject to undue risk as a consequence of payment schedules. In the negotiation of these agreements, CIRM recognizes that the selection of an appropriate royalty rate is required to successfully balance the expectation of the State of California for remuneration with the specific circumstances of the business position of the company. CIRM will use as its guide a royalty range of 2 to 5 percent as it negotiates the payment schedule for the expected capped return.

iv. Payback expectations for CIRM for-profit awardee organizations

Options for remuneration to the State of California include payment of an amount equivalent to that originally awarded, or an amount greater than that originally awarded. After researching best practices of entities that fund for-profit research organizations, empirical evidence was collected that suggests that requiring a return greater than that originally awarded does not present a *de facto* impediment to research progress. However, several funding organizations have reported that "uncapped" royalty expectations can have adverse effects on prospective for-profit sector awardees in later financing rounds and/or business development activities.

a. For CIRM for-profit awardees who develop CIRM-funded projects themselves

For-profit research organizations are structured to develop products for public benefit according to their research interests and business plans. As a consequence of this, it is likely that some CIRM for-profit awardees will intend to develop CIRM-funded projects for their own use rather than licensing rights to them to third parties. After extensive research, CIRM has developed proposed revenue sharing strategies to provide appropriate options in the best interests of the State of California. See figure 2 for a diagram of the revenue sharing structure.

i. Basic revenue sharing

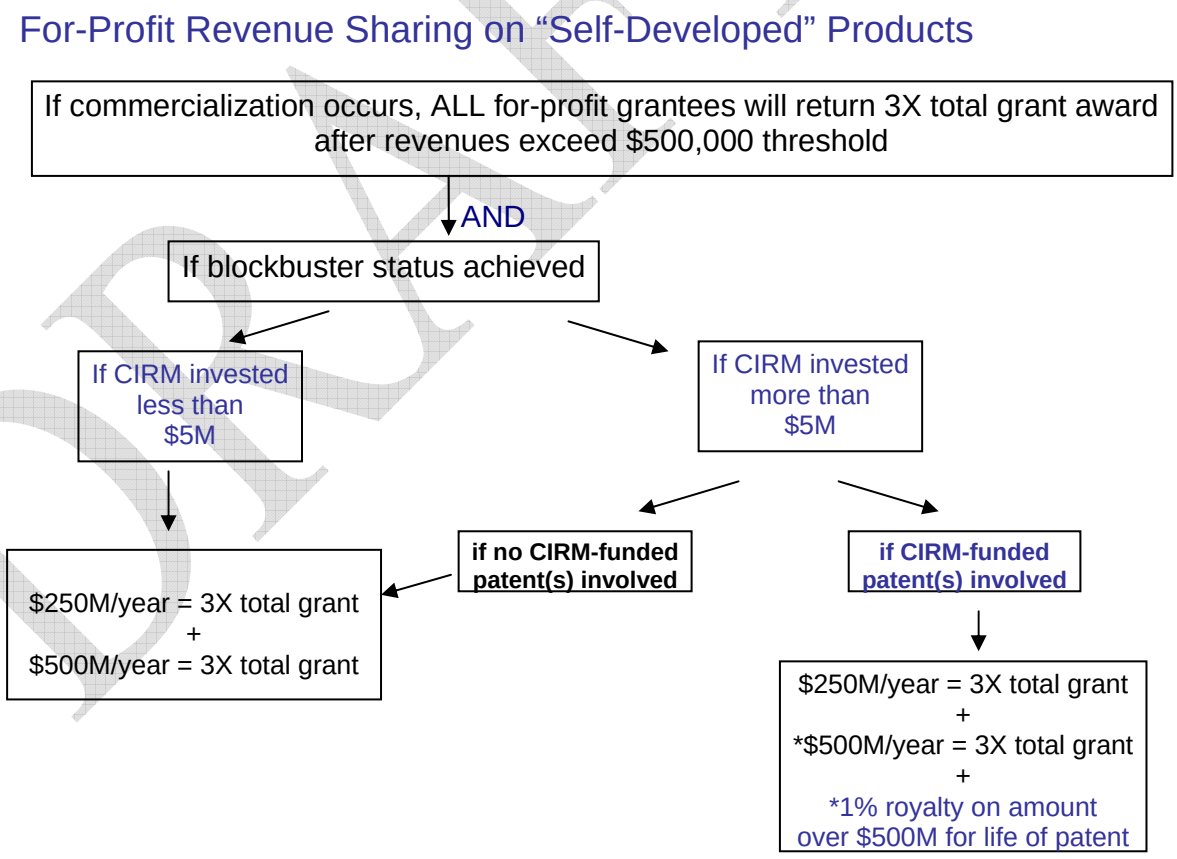
For grants made to for-profit organizations, the State of California will expect a return only in the event of successful commercialization of a product that stems from a CIRM-funded research project. Success will be defined as the receipt of revenues in excess of $500,000 from the CIRM-funded research-enabled product. In such cases, the State of California will receive three times the amount received under CIRM funding in the form of a capped royalty. For example, if CIRM awarded a $1 million grant that ultimately gave rise to a product that generates revenues, the State of California is expected to receive of a total of $3 million in royalty payments. The payment schedule will be negotiated using a royalty range of 2 to 5 percent to determine the rate at which the threefold return will be recovered.

ii. Blockbuster payments

For grants that lead to very successful commercial products, an additional one-time blockbuster payment equal to three times the amount provided by CIRM is expected each time revenues exceed a multiple of $250 million per year.

In the event that CIRM invested more than $5 million (in aggregate) and a CIRM-funded patented invention was involved in the achievement of blockbuster revenues in excess of $500 million per year, CIRM requires a 1 percent royalty on revenues in excess of $500 million for the life of the patent(s).

Figure 2:



iii. Access to resultant therapies developed by for-profit awardees
As a consequence of expenditure of the "first dollar" of CIRM funding, the for-profit awardee organization agrees to provide a plan to provide access at the time of commercialization to resultant therapies for uninsured California residents.

In addition, the awardees will provide the therapies at a discount price to residents whose therapies are purchased in California by public funds. For drugs generated as a consequence of CIRM funding, awardees agree to provide drugs at prices negotiated pursuant to the California Discount Prescription Drug Program (commencing with California Health and Safety Code section 130500, et seq.) to eligible Californians under that program. Awardees also agree to provide discount pricing for therapies in addition to drugs that result from CIRM funding.

In the unfortunate event of limited availability of therapeutic products resulting from CIRM funding, awardees agree to give preference to Californian residents unless prohibited by law and whenever feasible. If an awardee is unable to grant preference to Californian residents, the awardee agrees to submit a statement of justification to CIRM.

b. For CIRM for-profit awardees who license technology to third parties

Regulations from the CIRM *Intellectual Property Policy for Non-Profit Organizations* (IPPNPO) include provisions for licensing activities by non-profit organizations. In brief, the IPPNPO regulations were structured to allow a financial return on the public's research investment through the recovery of 25 percent of revenues from the non-profit grantee organization's (not the inventor's) share of revenues from licenses for CIRM-funded patented inventions. Consistent with their Bayh-Dole obligations, federally funded non-profit grantee organizations will share a fraction of revenues with the inventor(s) in accordance with their established practices. To defray administrative costs associated with patent expenses, CIRM will recover funds from a non-profit grantee organization when net revenues from a license or licenses of a CIRM-funded patented invention exceed $500,000 in the aggregate. In the event that CIRM partially funds research that leads to a licensed patented invention with revenues in excess of $500,000, the return to the State of California will be proportionate to the CIRM financial support.

On occasion, for-profit research organizations license their technologies to other companies. CIRM for-profit awardees who choose to license CIRM-funded

patented inventions to third parties will be subject to regulations similar to those approved for non-profit grantees with one exception. Since for-profit research organizations typically do not compensate inventors, an adjustment was made in the return expected as a consequence of revenues from licenses pertaining to CIRM-funded inventions. Universities typically share 30-40 percent of the "university share" with the inventor(s). In recognition of the differences between practices of non-profit and for-profit research organizations with respect to their payments to inventors, CIRM has proposed that the 25 percent return be reduced to 17 percent for for-profit awardees. This adjustment strives to provide an equal return to the General Fund from non-profit and for-profit grantees who license CIRM-funded patented inventions to third parties.

v. March-in rights for for-profit awardees

In an effort to ensure that CIRM-funded projects are brought to public use, CIRM maintains march-in rights for projects funded at for-profit research organizations. March-in rights provide CIRM with the right to require the awardee organization, or exclusive licensee of a CIRM-funded invention, to grant a nonexclusive, partially exclusive, or exclusive license in any field of use to a responsible applicant or applicants, upon terms that are reasonable under the circumstances, and if the awardee organization, or exclusive licensee refuses such request, to grant such a license itself, if the CIRM determines that such an action is required:

1. Because the awardee organization or the licensee has not made responsible efforts in a reasonable time to achieve practical application of a CIRM-funded patented invention;
2. Because the awardee or licensee has failed to adhere to the agreed-upon plan for access to resultant therapies;
3. To meet requirements for public use, including broad availability in California (for reasons other than price), and the requirements have not been satisfied by the awardee organization or its licensee;
4. To alleviate public health and safety needs which are not reasonably satisfied by the awardee organization or its licensee and which needs constitute a public health emergency.

CIRM will give to the awardee or licensee notice of such determination and the basis on which it was made. CIRM will not exercise its rights described above if the awardee or licensee takes diligent action promptly to cure the deficiency and such deficiency is cured sooner than one year from receipt of notice (or longer period by mutual agreement). With respect to a deficiency described in 4 (above), CIRM may exercise such right at any time in the event of a public health or safety emergency.

IV. Terms and Conditions for For-Profit Awardees

This section contains proposed terms and conditions with which awardee organizations and awardees must comply. Once finalized, these terms and conditions will comprise formal regulations that will be adopted by the ICOC pursuant to the Administrative Procedure Act. As with all regulations, these regulations will be binding on awardee organizations with the force and effect of law.

Note: The text in blue font differs from that approved by the ICOC for the CIRM Intellectual Property Policy for Non-Profit Organizations on February 10, 2006, and reflects language specific to the CIRM Policy for For-Profit Organizations.

A. Reporting Requirements

1. Awardee organizations must submit annual progress reports including scientific and financial statements during the period of the grant award.
2. Awardee organizations agree to disclose the filing of a patent application relevant to a CIRM-funded invention, and its application serial number. All disclosures of such inventions shall contain sufficient detail of the invention and shall be marked confidential in accordance with Health and Safety Code 125290.30, subdivision (e)(2)(B), and are therefore exempt from California Public Records Act.
3. Awardee organizations must notify CIRM regarding the issuance of patent applications, including the patent number and date of issuance, that claim inventions made in the performance of CIRM-funded research.
4. Awardee organization must notify CIRM regarding execution of any licensing agreements of patented inventions made in the performance of CIRM-funded research.
5. In the event of revenue streams created as a consequence of CIRM-funded patented inventions (whether from license agreements or self-commercialization activities), awardee organizations shall keep accurate records and accounts, and submit to CIRM a statement describing financial information relating to the CIRM-funded invention-related revenue stream for the preceding 12 month period. This information shall be marked confidential in accordance with

Health and Safety Code 125290.30, subdivision (e)(2)(B), and is therefore exempt from California Public Records Act.

B. Publication Requirements

1. Within 60 days of the publication of CIRM-supported research results in a scientific journal, Principal Investigators must submit to CIRM a 500 word abstract written for the general public that highlights the findings of the published body of work. In addition, PIs must submit a biographical sketch to accompany the abstract. The abstract and the biographical sketch will be deposited into the publicly-accessible CIRM Electronic Library Repository, to be accessed via the CIRM website.

2. One copy of each publication resulting from work performed under a CIRM grant must accompany the mandatory annual progress report submitted to CIRM.

3. In the final manuscript, authors must include the URL of a website where the CIRM Materials Transfer Agreement (or similar document) can be accessed to facilitate requests for publication-related materials.

4. CIRM awardees must acknowledge CIRM support of research findings in publications, announcements, presentations, and press releases by the awardees. An example of an acknowledgement is:

> "The research was made possible by a grant from the California Institute for Regenerative Medicine (Grant Number _____). The contents of this publication are solely the responsibility of the authors and do not necessarily represent the official views of CIRM or any other agency of the State of California."

C. Publication-Related Biomedical Materials Requirements

1. Unless a special case could be made to CIRM that doing so would endanger the competitive position of the company, an awardee shall share biomedical materials described in published scientific articles for research purposes in California within 60 days of receipt of a request and without bias as to the affiliation of the requestor unless legally precluded. Under special circumstances, exceptions to the above are possible with approval by CIRM; if requests become onerous or are in direct conflict with the business of the awardee, for-profit awardees

can appeal to CIRM for alternative arrangements. Alternatively, authors may provide requestors with information on how to reconstruct or obtain the material. Materials are to be shared without cost or at cost.

D. Patent Applications Requirements

1. Awardee organizations shall bear responsibility for costs associated with patents and patent applications claiming their CIRM-funded inventions.

2. Awardee organizations shall report filings of such patent applications, including the application serial number and issuances of patents, including the patent number and issuance date, that claim inventions made in the performance of CIRM-funded research. This information shall be marked confidential in accordance with Health and Safety Code 125290.30, subdivision (e)(2)(B), and is therefore exempt from the California Public Records Act.

E. Requirements for Licensing of CIRM-Funded Patented Inventions to Third Parties

1. Awardee organizations shall assume responsibility for licensing activities including identification of potential licensees, negotiation of license agreements and documentation of development progress for licenses relating to CIRM-funded patented inventions. Awardee organizations are required to submit a licensing activities report relevant to CIRM-funded patented inventions on an annual basis.

2. Awardee organizations shall negotiate non-exclusive licenses of CIRM-funded inventions to third parties whenever possible. Nevertheless, awardee organizations may negotiate and award exclusive licenses for CIRM-funded inventions if such licenses are necessary to provide economic incentives required to enable commercial development and availability of the inventions. In due diligence relating to such exclusive licenses, awardee organizations shall document development and commercialization capabilities of the intended licensee, and include terms in the license agreement addressing all relevant therapeutic and diagnostic uses for which the invention is applicable.

3. In exclusive license agreements, awardee organizations shall include terms for commercial development plans to bring the invention to practical application. Such provisions shall include commercial development milestones and benchmarks so that development can be assessed and monitored.

4. Awardee organizations shall grant exclusive licenses involving CIRM-funded patented inventions relevant to therapies only to organizations with plans to provide access at the time of commercialization to resultant therapies for uninsured California patients. In addition, such licensees will agree to provide to patients whose therapies will be purchased in California by public funds the therapies at a discount price. The CIRM may make access plans available for review by the ICOC.

5. Awardee organizations shall monitor the performance of exclusive licensees of CIRM-funded patented inventions to ensure that the licensed invention is developed in a timely fashion. Remedies for failure to develop may include modification or termination of a license in the event that a licensee is unable to fully develop the rights granted.

I. Awardee organizations shall negotiate relevant and specific grounds for modification or termination of the license. Examples would include failure to meet agreed-upon commercialization benchmarks, and failure to reasonably meet the agreed-upon plan for access to resultant therapies as described above in E(4) above.
II. Awardee organizations shall monitor the commercial development activities of the licensees to determine compliance with the terms of the license agreement and include reports of monitoring activities annually.
III. Awardee organizations shall take administrative action to modify or terminate license rights where necessary and report such action to the CIRM Scientific Program Officer.

F. Access Requirements for Products Developed by For-Profit Awardees:

1. The awardee organization will provide (at time of commercialization) to CIRM a plan to provide access to resultant therapies for uninsured Californians. The CIRM may make access plans available for review by the ICOC and the public.

2. Awardees agree to provide to patients whose therapies will be purchased in California by public funds the therapies at a discount price. For drugs generated as a consequence of CIRM funding, awardees agree to provide drugs at prices negotiated pursuant to the California Discount Prescription Drug Program (commencing with California Health and Safety Code section 130500, et seq.) to eligible Californians under that program. Awardees also agree to provide discount pricing for therapies in addition to drugs that result from CIRM funding.

3. In the unfortunate event of limited supply of therapeutic products generated as a consequence of CIRM funding, whenever feasible, awardees agree that preference will be given to California residents. If the awardee is unable to grant preference, the awardee agrees to submit a statement of justification to CIRM.

G. Revenue Sharing Requirements

1. In the event of the creation of revenue streams from CIRM-funded patented inventions licensed to third parties:

i. Awardee organizations shall share a fraction of any net revenues received in excess of $500,000 under a license agreement that involves CIRM-funded patented inventions. Net revenues are defined as gross revenues minus direct costs incurred in the generation and protection of the patents from which the revenues are received.

ii. The awardee organization may retain a threshold amount of its share of any revenues received under a license agreement or agreements of any CIRM-funded patented invention(s). The awardee organization shall pay 17 percent of its share of such revenues to the State of California for deposit into the State's General Fund unless such action violates any federal law. The threshold amount is $500,000 (in the aggregate) multiplied by a fraction, the denominator of which is the Consumer Price Index, All Urban Consumers, All Items (San Francisco-Oakland-San Jose; 1982-84=100) as prepared by the Bureau of Labor Statistics of the United States Department of Labor and published for the month of

_____ 2007, and the numerator of which is such Index published for the month in which the grant award is accepted by the awardee.

iii. If funding sources in addition to CIRM were used in the creation of a CIRM-funded patented invention, the return to the State of California of any resultant revenues shall be proportionate to the support provided by CIRM for the discovery of the invention. Awardees must submit calculations detailing CIRM's contribution to the invention. CIRM reserves the right to commission an audit of any expenditure funds provided by CIRM and all co-funding calculations.

2. In the event of the creation of revenue streams from self-commercialized products that result from CIRM-funded patented inventions:

i. Awardee organizations shall share revenues with the State of California (to be deposited into the State's General Fund) in the form of royalties capped at three times the total awarded money, adjusted as above using a Consumer Price Index calculation.

ii. Awardee organizations must submit calculations detailing CIRM's contribution to commercialization of the resultant product. CIRM reserves the right to commission an audit of any CIRM expenditure and all co-funding calculations.

3. In the event that revenues from CIRM-funded projects achieve blockbuster status: :

i. For grants that lead to very successful commercial products a one-time blockbuster payment equal to three times the original award(s) is expected each time revenues exceed a multiple of $250 million per year.

ii. In the event that CIRM invested more than $5 million (in aggregate) in the research project and a CIRM-funded patented invention was involved in the achievement of blockbuster revenues equivalent to or greater than $500 million per year, CIRM requires the payment of 1 percent of revenues in excess of $500 million for the life of the patent(s).

H. Press release requirements

CIRM awardees must notify CIRM prior to any press releases that refer to events that arise as a consequence of CIRM funding by contacting the CIRM Communications Officer.

I. March-in rights requirements

With regard to CIRM-funded patented inventions or CIRM-funded research projects, CIRM shall have the right to require the awardee organization, or exclusive licensee of a CIRM-funded invention, to grant a nonexclusive, partially exclusive, or exclusive license in any field of use to a responsible applicant or applicants, upon terms that are reasonable under the circumstances, and if the awardee organization, or exclusive licensee refuses such request, to grant such a license itself, if the CIRM determines that such an action is required:

1. Because the awardee organization or the licensee has not made responsible efforts in a reasonable time to achieve practical application of a CIRM-funded patented invention;
2. Because the awardee or licensee has failed to adhere to the agreed-upon plan for access to resultant therapies;
3. To meet requirements for public use including broad availability in California (for reasons other than price), and the requirements have not been satisfied by the awardee organization or its licensee;
4. To alleviate public health and safety needs which are not reasonably satisfied by the awardee organization or its licensee and which needs constitute a public health emergency.

CIRM will give notice of such determination and the basis on which it was made to the awardee or licensee. CIRM will not exercise its rights described above if the awardee or licensee takes diligent action promptly to cure the deficiency and such deficiency is cured sooner than one year from receipt of notice (or longer period by mutual agreement). With respect to a deficiency described in I.4., CIRM may exercise such right at any time in the event of a public health or safety emergency.

V. Partial List of References

Technology transfer and the public interest: Cooperative Research and Development Agreements at NIH (1993 report by the Department of Health and Human Services Office of the Inspector General)

http://oig.hhs.gov/oei/reports/oei-01-92-01100.pdf#search=%22fair%20pricing%20clause%20CRAD%22

Government-Industry Partnerships for Development of New Technologies (2002)
Board on Science, Technology, and Economic Policy (STEP)

http://darwin.nap.edu/books/0309085020/html/11.html

CRADA abolition of pricing clause:

http://www.bioinfo.com/reasprice.html

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VI. Appendix 1

Working draft: **Funding Source Table**

Funding Source	Funds For-Profit?	Repayment Expectation?	Range
Federal Programs			
SBIR	Yes	No	$100,000-750,000
STTR	Yes	No	$100,000-750,000
ATP	Yes	No	$400,000-31,000,000
State Tech Programs			
MD: TEDCO	Yes	Yes	$15,000-30,000
PA: Ben Franklin	Yes	Yes	$5,000-250,000
CA: UCDiscovery	Yes	No	$50,000-3,000,000
CA: SRP BCRP	Yes	No	~$100,000-400,000
State Stem Cell Programs			
CT	No	Yes	$200,000 – 3,800,000
IL	No	?	?
MD	Yes	?	?
NJ	Yes	Yes	$300,000
Foundations/Organizations			
AmHeartAssociation	No	Yes	
AmCancerSociety	No	Yes	
CysticFibrosisFoundation	Yes	Yes	
CancerResearchUK	Yes	Yes	
GatesFoundation	No	No	
HHughesMedInstitute	No	Yes	
JuvDiabetesResFound	Yes	Yes	
StanleyMedResInstitute	Yes	Yes	
WellcomeTrust	Yes	Yes	